Recurrent severe symptomatic hyponatraemia induced by low-dose oral cyclophosphamide in a patient with ANA-related vasculitis.

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Introduction

- Cyclophosphamide is an alkylating agent used in the treatment of malignant and autoimmune diseases.
- Severe hyponatraemia is a serious electrolyte disorder with life threatening neurological sequelae.
- It has been reported in association with a variety cytotoxic agents as vinca alkaloids, platinum compounds and alkylating agents.[1]
- Severe hyponatraemia after administration of low-dose cyclophosphamide therapy (<15 mg/kg) is extremely rare.

Clinical Presentation

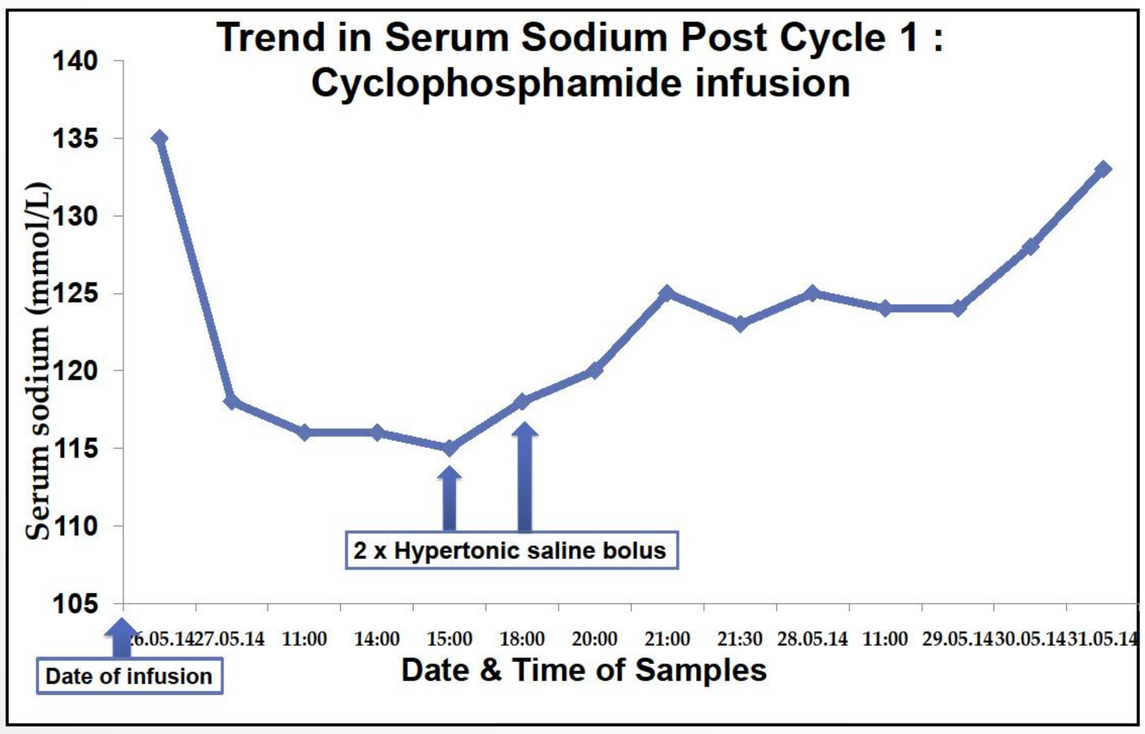
- **61** year old lady commenced on intravenous cyclophosphamide for mononeuritis mulitplex

Medical History:

- ANA positive systemic vasculitis
- Sjogrens syndrome
- Osteoarthritis
- Multinodular Goitre

First Cycle- May 2014

- Low dose cyclophosphamide, 620mg (12.5mg/kg).
- Oral mesna pre & post infusion.
- Oral Ondansetron 8mg pre & post infusion.
- Prehydration ; **1L 0.9% saline**
  3L of H_2O to prevent haemorrhagic cystitis.



Investigations

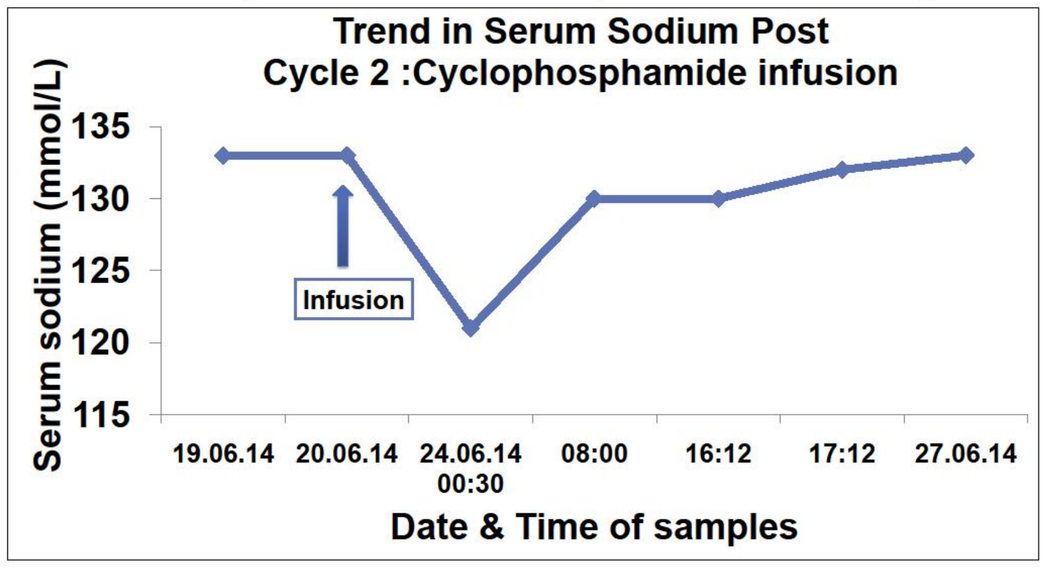
Serum Osmolality	240mOsm/kg
Urine Osmolality	347 mOsm/kg
Urinary Sodium	121mmol/L
8am Cortisol	800nmol/l
FT4	15.4pmol/l
TSH	1.04mIU/L

Management

- 24hrs post infusion, at a serum sodium of 116mmol/L, she was nauseous, drowsy and slurring her speech.
- She was transferred to ITU.
- Given stat dose of 100ml of **3% saline**.
- Her sodium rose from **115mmol/L to 118mmol/L.**
- Persistent clinical evidence of cerebral irritation hence given another 100ml of **3% saline**.
- Serum sodium rise **118mmol/l to 120mmol/l.**
- Within 48hrs her serum sodium rose to 125mmol/L.
- She recovered without any neurological deficits.

Second Cycle- June 2014

- Low dose cyclophosphamide,
- Reduced Prehydration; **N0 IV saline,** Consumed **2L of H_2O.**



- 12hrs post infusion, her serum sodium fell to 121mmol/l without neurological symptoms
- Placed on fluid restriction of 1.5L with gradual rise in serum sodium

Third Cycle- July 2014

- Low dose cyclophosphamide
- **NO prehydration**
- **1.5L fluid restriction**
- **Fall in serum sodium from 135mmol/L to 129mmol/l**
- No neurological symptoms
- Spontaneous correction

Conclusion

- Patients receiving cyclophosphamide are at high risk of developing symptomatic hyponatraemia due to SIADH even at low doses of therapy.
- Cyclophosphamide may induce SIADH, by potentiating the renal actions of AVP[2].
- The combination of both increased ADH effect and excess water intake to prevent haemorrhagic cystitis can induce potentially life-threatening hyponatraemia[3].
- Clinicians need to be aware of this threat when encouraging large volume prehydration and diuresis with cyclophosphamide therapy.
- It is possible that pre-hydration with isotonic saline rather than oral water may minimise the incidence of this complication

References

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Clinical Cases - thyroid/others
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